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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,726	11/28/2000	Gyula Hadlaczky	24601-402E	7776
20985	7590	08/12/2004	EXAMINER	
FISH & RICHARDSON, PC 12390 EL CAMINO REAL SAN DIEGO, CA 92130-2081			HELMER, GEORGIA L	
			ART UNIT	PAPER NUMBER
			1638	
DATE MAILED: 08/12/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/724,726

Applicant(s)

HADLACZKY ET AL.

Examiner

Georgia L. Helmer

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 April 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 50-52 and 55-57 is/are pending in the application.
- 4a) Of the above claim(s) 55-57 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 50-52 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- 1) ☐ Certified copies of the priority documents have been received.
 - 2) ☐ Certified copies of the priority documents have been received in Application No. _____.
 - 3) ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>22April2004</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Claims

1. The Office acknowledges receipt of Applicants Response; dated 22 April 2004, and of the 37 CFR 1.132 Declaration of Steven Fabijanski dated 19 January 2004. This 37 CFR 1.132 Declaration of Steven Fabijanski is the second 1.132 declaration of Fabijanski in this case, the first dated 16 July 2003. Hereafter this second declaration is referred to as "Fabijanski Declaration 2".
2. Claims 50-52 are pending and are examined in this Office Action. The Office inadvertently previously omitted listing claims 55-57 as pending and withdrawn as nonelected claims. Claims 55-57 are pending. Claims 58-61, 65-67 and 72 were cancelled in Applicant's response dated 22 July 2003. The claims filed 4 October 2003 do not reflect this. Applicant is kindly requested to file a new copy of the pending claims.
3. This application contains claims 55-57 drawn to an invention nonelected with traverse in papers filed 01 November 2002. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.
4. Applicant's attention is drawn to the Office Action of 03 October 2002, renumbering of claims under 35 CFR 1.162. Previous claims 52 and 53 were claims 51 and 52, according to 37 CFR 1.162.
5. This action is made FINAL.
6. All rejections not addressed below have been withdrawn.

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7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

8. An initialed and dated copy of Applicant's IDS form 1449 (26 April 2004) is attached to the instant Office action.

Claim Rejections - 35 USC § 112-second

9. Claims 50-52 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons of record. This rejection is repeated for reasons of record as set forth in the Office Action mailed 22 October 2003. Applicant's arguments filed 22 April 2004 have been fully considered but are not deemed persuasive..

At claim 50, line 2, the term "satellite artificial chromosome" is unclear.

What is a satellite artificial chromosome?

Applicant traverses saying primarily that Applicant has discovered something new that no name existed to describe, citing the examples of the first automobile or telephone (Response, p. 4). Applicant's traversal is unpersuasive. The first automobile and the first telephone were clearly described by drawings and figures and included working models of the inventions

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Applicant recites various qualities of an satellite artificial chromosome:

- it contains "satellite DNA" (specification, p. 5). What is "satellite DNA" and how does it differ from other DNA?
- it is a "fully functional stable chromosome" (specification, p. 5).
- it provides an extra genomic locus for targeted integration of DNA (specification, p. 5).
- it is primarily made up of "repeating units of short satellite DNA" and are "nearly fully heterochromatic" (specification, p. 7). What does "nearly fully" mean? 50%? 90%?

Applicant traverses saying primarily with respect to the terms "fully functional stable chromosome", "the elements of a functional, stable artificial chromosome" are provided in the specification at page 10, and "include a centromere, two telomeres, at least one origin of replication and filler heterochromatin" (Response, p. 7). Applicant's traversal is unpersuasive. Applicant has not addressed the difference between "a fully functional stable chromosome" and a "functional, stable artificial chromosome". Applicant further has provided no structural information re what is the linear order "a centromere, two telomeres, at least one origin of replication and filler heterochromatin" or what the relationship of one to the other is.

Applicant traverses saying primarily that terms "nearly fully heterochromatic" are defined on page 7 of the specification to mean "so that without insertion of heterologous or foreign DNA, the chromosomes preferably

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contain no genetic information or contain only non-protein encoding gene sequences such as rDNA" (Response, p.8). Applicant's traversal is unpersuasive. Since the elements of a functional, stable artificial chromosome include a centromere, two telomeres, at least one origin of replication as discussed above, how can the SATAC have no genetic information?

However a recitation of properties of a satellite artificial chromosome does not teach what the essential elements of satellite artificial chromosome are, nor does this make the metes and bounds of satellite artificial chromosome apparent.

Applicant traverses saying primarily (response, p. 8) that since the term SATAC is recited in an issued claim (US 6,077,697), this term is presumptively definite (response, p. 8). Applicant's traversal is unpersuasive. Each case is different and is evaluated on its own merit.

Claim Rejections - 35 USC § 112 Written Description

10. Claims 50-52 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for reasons of record. This rejection is repeated for reasons of record as set forth in the Office Action mailed 22 October 2003. Applicant's arguments filed 22 April 2004 have been fully considered but are not deemed persuasive.

Applicant traverses asserting the specification provides detailed definitions and structural characterizations of a SATAC and each of its elements so that it is clear that Applicant was in possession of a SATAC as of the filing date of the

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instant application and as of its earliest priority date. Applicant further says the specification describes how plant artificial chromosome differs from other artificial chromosomes (Response, p. 12): “a mammalian artificial chromosome (MAC) is a piece of DNA that can stably replicate and segregate alongside endogenous chromosomes. It has the capacity to accommodate and express heterologous genes inserted therein. It is referred to as a mammalian artificial chromosome because it includes an active mammalian centromere. Plant artificial chromosome..refer to chromosomes that include plant..centromeres” (specification, p. 16). Applicant's traversal is unpersuasive. Applicant defines the artificial chromosome as being a piece of DNA having certain qualities. However Applicant's definition and description is given in terms of “chromosomes”. Chromosomes consist of nucleic acids and proteins, the proteins being histone proteins as well as non-histone proteins, not naked DNA. It would appear that Applicant's description of artificial chromosome, as DNA, is lacking at least one family of components—the proteins. Furthermore, describing a artificial chromosome as DNA that can stably replicate and segregate alongside endogenous chromosomes, and having the capacity to accommodate and express heterologous genes inserted therein, fails to distinguish artificial chromosome from “wild-type” chromosomes. “Wild-type” chromosomes can stably replicate and segregate alongside endogenous chromosomes, and have the capacity to accommodate and express heterologous genes inserted therein, as is known from the literature, which abounds with examples of transgenic animals, fungi and plants, and many progeny generations of these transgenics.

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Applicant traverses saying primarily that the instant Application provides exemplary SATACs evidencing Applicant possession of the claimed subject matter (Response, p. 14). Applicant says that the specification describes the generation of cell lines such as G3D5 and HID3 containing megachromosomes (exemplary SATACs), and that these cells lines have been deposited in the ECACC and gives accession numbers. Applicant argument is unpersuasive. Overcoming a written description rejection under 112.1 cannot be overcome by deposit of biological material, even though such a biological deposit may be relevant to an 112.1 Enablement requirement. Applicant further asserts that the specification depicts the structures of SATACs schematically in Figures 2 and 3 of the specification (Response, p. 15). Applicant's assertion is unpersuasive. Figures 2 and 3 show schematic of complex macromolecular pathway starting with mouse chromosome #7 being transfected with foreign DNA, which DNA is described as specific λ DNA. The other components are macromolecular complexes, comprising for example heterochromatin and euchromatin.

Applicant, noting that the instant Application is a CIP of US 6,077,697, which contains issued claims directed to methods of producing and isolating SATAC as well as composition claims directed to isolated SATACs, and therefore provides SATACs and their structural elements. Applicant's assertion is unpersuasive. Each case is different.

Applicant fails to provide Written Description with respect to the structural and physical characteristics of the claimed invention. There is no structural description, other than saying that a SATAC is a piece of DNA, of what

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comprises a SATAC . Applicant fails to mention or describe in any way, other required components, namely the proteins. Therefore Applicant is claiming a genus of macromolecular components, yet there is not description to the structural features that define the genus.

Claim Rejections - 35 USC § 112.1 Enablement

11. Claims 50-52 remain rejected under 35 U.S.C. 112, first paragraph, for reasons of record. This rejection is repeated for reasons of record as set forth in the Office Action mailed 22 October 2003. Applicant's arguments filed 22 April 2004 have been fully considered but are not deemed persuasive.

The Declaration of Fabijanski (Fabijanski Declaration 1) has been thoroughly considered and is found not to be commensurate in scope with the scope of the claims. Affiant Fabijanski states that "using methods and materials described in the...application and standard methods described herein", he and other project scientists have demonstrated that SATAC can be transferred to plant protoplasts, using microcell-mediated fusion of SATAC containing murine (mouse) cells with plant protoplasts, and lipid-mediated transfection of isolated SATAC into plant protoplasts (Declaration p. 2). Applicant asserts_ that the Fabijanski Declaration states (Declaration, pages 2-5) that the following experiments have been done by him: (a) the transfer of a mouse SATAC into tobacco cells using microcell-mediated fusion, (b) the transfer of a mouse SATAC into Arabidopsis cells using microcell-mediated fusion, and (c) the

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transfer of a mouse SATAC into rice protoplasts (using protocols of US 6,077,697) using lipid-mediated transfection. Applicant concludes that SATACs can be transferred to plant cells. Applicant's traversal has been considered and is unpersuasive because the Declaration is lacking any teaching of a SATAC in a transformed plant, the claimed invention.

The Declaration of Fabijanski, dated 19 January 2004, (Fabijanski Declaration 2) as been thoroughly considered and is found not to be commensurate in scope with the scope of the claims.

Fabijanski describes (Declaration 2 p. 5 last ¶ - p. 10) the "generation of plant artificial chromosomes (Plant SATACs)" by (1) construction of heterologous DNAs—(a) a vector DNA containing a region of homology to tobacco pericentric DNA and a detection marker containing mouse satellite DNA, and (b) a second DNA, the "targeting DNA" containing a region of homology to pericentric DNA sequences; (2) introduction of the DNAs into plant cells and selection—(c) by introduction of Vector DNA and targeting DNA into tobacco protoplasts using transfection, followed by culture of plant tissue microcalli under selective antibiotic conditions. (d) Resulting selected calli were subjected to image analysis using probes specific to the detection marker and to the pericentric sequences. (e) Identification of large scale vector amplification (Declaration, p. 9), followed by (f) overlap image analysis, followed by further analysis.

Fabijanski states (that these experiments show "the production of two amplified regions as a result of insertion of vector DNA into the pericentric DNA

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and evidence for large scale amplification, including "sausage" amplification. A SATAC produced from a breakage product was identified that contained amplified vector DNA as well as heterochromatic DNA. The callus line containing the plant SATAC was stably maintained in culture for over 6 months" (Declaration p.6-7). The Declaration of Fabijanski, which provides information of the creation of a plant SATAC, is not commensurate in scope with the scope of the claims. None of the claims is drawn to a SATAC comprising plant amplified vector DNA and well as heterochromatic DNA. The claims are drawn to method of producing a transgenic plant comprising introducing a SATAC into a plant protoplast and growing the protoplast under conditions to produce a transgenic plant.

Furthermore, it is not clear that the methods used by Fabijanski in this work are the methods disclosed in the specification as filed.

Applicant has shown data for introducing of a mouse SATAC into a protoplast of tobacco and of Arabidopsis. No guidance is given for growing a SATAC containing protoplast into a transgenic plant. Wild-type plant cells do not normally have SATACs. No information or guidance is given for the conditions, including the specific cells, of what explants of a plant, of what plants, comprising "SATACs" containing what native DNA and what foreign DNA, what origin of replication from what kind cell of what kind of organism, and what centromere, from what cell of what kind of organism, would function as desired to produce the transgenic plant transgenic for the SATAC. Applicant must provide sufficient guidance to address these issues. Without such guidance the experimentation

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required would not be routine, but would be undue. This would impose a burden on the skilled artisan, without a reasonable expectation of success.

Applicant is not enabled for the claimed invention as commensurate in scope with the claims

Remarks

12. No claims are allowed.

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

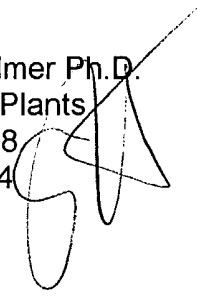
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Georgia L. Helmer whose telephone number is 571-272-0796. The examiner can normally be reached on 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 571-272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Georgia Helmer Ph.D.
Transgenic Plants
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21 July 2004



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